Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	5571	cunningham.in. or Wayne-State$.as.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L2	0	garrett-roger$.in. and "ribosome binding"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L3	18	garrett-roger$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L4	6210	ribosomal ADJ RNA	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L5	23530	site-directed ADJ mutagenesis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L6	16047	antibiotic ADJ resistance	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L7	137	rRNA ADJ operon	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L8	17100	(message or ribosome) ADJ "binding site"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L9	5533	"shine dalgarno"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L10	14	anti ADJ L9	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L11	28	SD WITH ASD	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L12	2	L11 and L4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59

L13	1	complementary WITH "mutant shine"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L14	3	mutant ADJ L9	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L15	6840	L6 and L8	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L16	2478	L15 and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L17	9	L16 and L7	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L18	11936	L4 or "rRNA"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L19	2255	L18 and L5	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L20	7	L18 SAME L5	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L21	3	functional WITH "mutant ribosome"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L22	0	multiresistance SAME "drug screen"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L23	0	multi-resistance SAME "drug screen"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L24	1	multidrug SAME "drug screen"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59

L25	19	"mutant ribosome"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L26	7	L1 and L4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L27	239	drug SAME (target ADJ RNA)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L28	58	L27 and L4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L29	1	L28 and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L30	58	L27 and L4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L31	0	L28 and "anti shine"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L32	5652	anti ADJ infect$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L33	19	L32 and L9	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L34	6	L33 and L4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L35	4	mutat$ ADJ L9	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/29 16:59
L36	0	"16s" ADJ mutation	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/29 17:46

L37	1009	"16S" ADJ ribosom$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/29 17:46
L38	9	l37 WITH mutation	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/29 17:53
L39	5492	antibiotic WITH drug	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/29 17:53
L40	9	l37 WITH human	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/04/29 17:54

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     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 18:07:27 ON 29 APR 2005
L1         11361 S 16S (2W) RIBOSOM?
L2           155 S L1 (S) MUTAT?
L3            32 S L2 AND ANTIBIOTIC
L4            27 S L3 NOT PY>=2003
L5            16 DUP REM L4 (11 DUPLICATES REMOVED)
L6             0 S L5 AND SCREEN
L7           951 S DRUG (3W) SCREEN
L8             8 S L7 AND ANTIBIOTIC
L9             6 DUP REM L8 (2 DUPLICATES REMOVED)
L10       379960 S ANTIBIOTIC
L11          138 S L1 (S) HUMAN
L12            4 S L11 AND L10
L13            2 DUP REM L12 (2 DUPLICATES REMOVED)
L14          175 S L1 (S) BINDING
L15           35 S L14 AND L10
L16           31 S L15 NOT PY>=2003
L17           18 DUP REM L16 (13 DUPLICATES REMOVED)
L18           18 S L17 AND (DRUG OR ANTIBIOTIC)
L19       661154 S CUNNINGHAM?/AU OR LEE?/AU OR DEBOER?/AU OR GREEN?/AU OR MORGA
L20          299 S L19 AND L1
L21           18 S L20 AND L10
L22           12 S L21 NOT PY>=2003
L23            2 S L22 AND L2
L24           10 DUP REM L22 (2 DUPLICATES REMOVED)
L25            0 S SELECT? ADJ MARKER
L26         8004 S SELECT? (2W) MARKER
L27          623 S RIBOSOM? (2W) MUTAT?
L28            0 S L27 AND L26
L29           49 S L26 AND RRNA
L30           45 S L29 NOT PY>=2003
L31           20 DUP REM L30 (25 DUPLICATES REMOVED)
L32            8 S (MUTATED OR MUTANT) (3W) DALGARNO
L33            3 DUP REM L32 (5 DUPLICATES REMOVED)
L34           14 S (MUTATED OR MUTANT) (5W) DALGARNO
L35            0 S L34 AND L26
L36            0 S L34 AND (MARKER OR REPORTER)
L37           10 DUP REM L24 (0 DUPLICATES REMOVED)

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 18:35:36 ON 29 APR 2005
L38           14 S (MUTATED OR MUTANT) (6W) DALGARNO
L39            6 DUP REM L38 (8 DUPLICATES REMOVED)
L40         1833 S CODON (P) ANTICODON
L41           11 S L40 AND L27
L42            6 DUP REM L41 (5 DUPLICATES REMOVED)
L43            1 S L42 AND L10

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L43 ANSWER 1 OF 1 MEDLINE on STN

ACCESSION NUMBER: 1999134386 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9931247
TITLE: Effect of mutations in the A site of 16 S rRNA on aminoglycoside **antibiotic**-ribosome interaction.
AUTHOR: Recht M I; Douthwaite S; Dahlquist K D; Puglisi J D
CORPORATE SOURCE: Department of Structural Biology, Stanford University School of Medicine, Stanford, CA, 94305-5126, USA.
CONTRACT NUMBER: GM51266 (NIGMS)
SOURCE: Journal of molecular biology, (1999 Feb 12) 286 (1) 33-43.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990413
Last Updated on STN: 19990413
Entered Medline: 19990329

AB Decoding of genetic information occurs upon interaction of an mRNA **codon**-tRNA **anticodon** complex with the small subunit of the ribosome. The ribosomal decoding region is associated with highly conserved sequences near the 3' end of 16 S rRNA. The decoding process is perturbed by the aminoglycoside antibiotics, which also interact with this region of rRNA. Mutations of certain nucleotides in rRNA reduce aminoglycoside binding affinity, as previously demonstrated using a model RNA oligonucleotide system. Here, predictions from the oligonucleotide system were tested in the **ribosome** by **mutation** of universally conserved nucleotides at 1406 to 1408 and 1494 to 1495 in the decoding region of plasmid-encoded bacterial 16 S rRNA. Phenotypic changes range from the benign effect of U1406-->A or A1408-->G substitutions, to the highly deleterious 1406G and 1495 mutations that assemble into 30 S subunits but are defective in forming functional ribosomes. Changes in the local conformation of the decoding region caused by these mutations were identified by chemical probing of isolated 30 S subunits. Ribosomes containing 16 S rRNA with mutations at positions 1408, 1407+1494, or 1495 had reduced affinity for the aminoglycoside paromomycin, whereas no discernible reduction in affinity was observed with 1406 mutant ribosomes. These data are consistent with prior NMR structural determination of aminoglycoside interaction with the decoding region, and further our understanding of how aminoglycoside resistance can be conferred.

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L39 ANSWER 1 OF 6 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002484669 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12270836
TITLE: Pseudoknot-dependent translational coupling in repBA genes of the IncB plasmid pMU720 involves reinitiation.
AUTHOR: Praszkier J; Pittard A J
CORPORATE SOURCE: Department of Microbiology and Immunology, The University of Melbourne, Victoria 3010, Australia.. judy@ariel.its.unimelb.edu.au
SOURCE: Journal of bacteriology, (2002 Oct) 184 (20) 5772-80. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020925
Last Updated on STN: 20021029
Entered Medline: 20021028

AB Replication of the IncB miniplasmid pMU720 requires synthesis of the replication initiator protein, RepA, whose translation is coupled to that of a leader peptide, RepB. The unusual feature of this system is that translational coupling in repBA has to be activated by the formation of a pseudoknot immediately upstream of the repA Shine-Dalgarno sequence. A small antisense RNA, RNAI, controls replication of pMU720 by interacting with repBA mRNA to inhibit expression of repA both directly, by preventing formation of the pseudoknot, and indirectly, by inhibiting translation of repB. The mechanism of translational coupling in repBA was investigated using the specialized ribosome system, which directs a subpopulation of ribosomes that carry an altered anti-Shine-Dalgarno sequence to translate mRNA molecules whose Shine-Dalgarno sequences have been altered to be complementary to the **mutant** anti-Shine-**Dalgarno** sequence. Our data indicate that translation of repA involves reinitiation by the ribosome that has terminated translation of repB. The role of the pseudoknot in this process and its effect on the control of copy number in pMU720 are discussed.

L39 ANSWER 2 OF 6 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 95118366 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7818544
TITLE: Synthesis of non-translating or translating specialized ribosomes causes feedback regulation of ribosomal RNA synthesis in Escherichia coli.
AUTHOR: Leipold R J; Morgan R W; Dhurjati P
CORPORATE SOURCE: Department of Chemical Engineering, University of Delaware, Newark 19716.
SOURCE: Biochemical and biophysical research communications, (1995 Jan 5) 206 (1) 393-400. Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950217
Last Updated on STN: 19950217
Entered Medline: 19950209

AB Specialized ribosomes carry a **mutant** anti-Shine-**Dalgarno** region that disrupts the complementary base pairing that stabilizes the translation initiation complex with E. coli mRNAs. It has been reported that production of specialized ribosomes does not cause the inhibition of chromosomal rRNA synthesis that follows production of wild-type ribosomes. We proposed that enabling translation on specialized ribosomes by providing mRNA with a complementary mutation in the Shine-Dalgarno region would restore feedback regulation and inhibit chromosomal rRNA synthesis. With both our system and the system studied previously, we saw feedback regulation regardless of whether the specialized ribosomes were

translating. As reported previously, transcription from plasmid-borne promoters decreased as chromosomal rRNA synthesis was repressed, suggesting that the lambda PL and tac promoters may be sensitive to the effector(s) of feedback regulation.

L39 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 87260869 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2440027
TITLE: A single base change in the Shine-Dalgarno region of 16S rRNA of Escherichia coli affects translation of many proteins.
AUTHOR: Jacob W F; Santer M; Dahlberg A E
CONTRACT NUMBER: GM19756 (NIGMS)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1987 Jul) 84 (14) 4757-61.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198708
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19870820

AB A single base mutation was constructed at position 1538 of Escherichia coli 16S rRNA, changing a cytidine to a uridine. This position is in the Shine-Dalgarno region, thought to be involved in base-pairing to mRNA during initiation of protein synthesis. The mutation was constructed by using a synthetic oligodeoxynucleotide that differs in sequence by one base from the wild-type sequence of 16S rRNA. This oligonucleotide was used as a primer on single-stranded DNA of phage M13, into which was cloned a specific region of DNA encoding 16S rRNA. The mutation is lethal when expressed from the normal promoters of rRNA operons, P1 and P2, in a high-copy-number plasmid. Expression can be repressed by a temperature-sensitive repressor, cI857, in combination with the bacteriophage lambda PL promoter. Induction of transcription by temperature shift yields mutant 16S rRNA that is processed and assembled into functional ribosomal subunits. The presence of mutant ribosomes retards cell growth and dramatically alters incorporation of [35S]methionine into a large proportion of the cellular proteins. The change in level of synthesis of individual proteins correlates with the change in base-pairing between **mutant** rRNA and the Shine-**Dalgarno** region of the mRNA.

L39 ANSWER 4 OF 6 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 88038329 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2823057
TITLE: Partitioning of the F plasmid: overproduction of an essential protein for partition inhibits plasmid maintenance.
AUTHOR: Kusukawa N; Mori H; Kondo A; Hiraga S
CORPORATE SOURCE: Institute for Virus Research, Kyoto University, Japan.
SOURCE: Molecular & general genetics : MGG, (1987 Jul) 208 (3) 365-72.
Journal code: 0125036. ISSN: 0026-8925.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198711
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19871130

AB Multicopy plasmids carrying the sopB gene of the F plasmid inhibit stable inheritance of a coexisting mini-F plasmid. This incompatibility, termed IncG, is found to be caused by excess amounts of the SopB protein, which is essential for accurate partitioning of plasmid DNA molecules into daughter cells. A sopB-carrying multicopy plasmid that shows the IncG+

phenotype was mutagenized in vitro and IncG negative mutant plasmids were isolated. Among these amber and missense mutants of sopB, mutants with a low plasmid copy number and a **mutant** in the Shine-**Dalgarno** sequence for translation of the SopB protein were obtained. These results demonstrate that the IncG phenotype is caused by the SopB protein, and that the incompatibility is expressed only when the protein is overproduced. This suggests that the protein must be kept at appropriate concentrations to ensure stable maintenance of the plasmid.

L39 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 85237481 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3892012
TITLE: Point mutations that affect translation initiation in the Escherichia coli gal E gene.
AUTHOR: Dreyfus M; Kotlarz D; Busby S
SOURCE: Journal of molecular biology, (1985 Apr 5) 182 (3) 411-7. Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198508
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19850801

AB This paper describes the selection and characterization of several mutations in the Escherichia coli galactose operon that affect translation initiation of the galE gene but are located outside of the Shine-Dalgarno sequence and the initiator codon. One mutation lies in the gal promoter region and shifts transcription initiation from the galP1 to the galP2 promoter. This results in a gal messenger that is five nucleotides longer and that is translated threefold more efficiently in vivo. This accords with previous observations from in vitro experiments which showed that the longer gal messenger was better translated (Queen & Rosenberg, 1981). The other mutations that affect galE translation are located in the coding sequence immediately downstream from the initiator codon. In contrast to the promoter mutation, these cause alterations in galE expression only when the gene carries a **mutated** initiator codon or Shine-**Dalgarno** sequence and have no effect on the wild-type galE gene. These findings are discussed with respect to our present knowledge of translation initiation mechanisms.

L39 ANSWER 6 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1984:354857 BIOSIS
DOCUMENT NUMBER: PREV198478091337; BA78:91337
TITLE: XYLOSE ISOMERASE FROM ESCHERICHIA-COLI CHARACTERIZATION OF THE PROTEIN AND THE STRUCTURAL GENE.
AUTHOR(S): SCHELLENBERG G D [Reprint author]; SARTHY A; LARSON A E; BACKER M P; CRABB J W; LIDSTROM M; HALL B D; FURLONG C E
CORPORATE SOURCE: GENETICS DEPARTMENT, SK-50, UNIVERSITY OF WASHINGTON, SEATTLE, WASHINGTON 98195, USA
SOURCE: Journal of Biological Chemistry, (1984) Vol. 259, No. 11, pp. 6826-6832. CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The gene that codes for xylose isomerase in E. coli was cloned by complementation of a xylose isomerase-negative E. coli mutant. The structural gene is 1320 nucleotides in length and codes for a protein of 440 amino acids. An additional 209 nucleotides 5' and 82 nucleotides 3' to the structural gene were also sequenced. To verify that the cloned gene encodes E. coli xylose isomerase, the enzyme was purified to homogeneity and the sequence of the first 25 amino acid residues was determined by a semimicromanual Edman procedure. The NH2-terminal methionine of xylose isomerase is specified by an ATG which is 7 nucleotides downstream from a Shine-Dalgarno sequence.

L18 ANSWER 1 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2001539527 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11587639
TITLE: Crystal structure of paromomycin docked into the eubacterial ribosomal decoding A site.
AUTHOR: Vicens Q; Westhof E
CORPORATE SOURCE: Institut de Biologie Moleculaire et Cellulaire du CNRS, Modelisation et simulations des Acides Nucleiques, UPR 9002, 15 rue Rene Descartes, Cedex 67084, Strasbourg, France.
SOURCE: Structure (Cambridge, Mass. : 2001), (2001 Aug) 9 (8) 647-58.
Journal code: 101087697. ISSN: 0969-2126.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1J7T
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011008
Last Updated on STN: 20020122
Entered Medline: 20011207

AB BACKGROUND: Aminoglycoside antibiotics interfere with translation in both gram-positive and gram-negative bacteria by **binding** to the tRNA decoding A site of the **16S ribosomal** RNA. RESULTS: Crystals of complexes between oligoribonucleotides incorporating the sequence of the ribosomal A site of Escherichia coli and the aminoglycoside paromomycin have been solved at 2.5 A resolution. Each RNA fragment contains two A sites inserted between Watson-Crick pairs. The paromomycin molecules interact in an enlarged deep groove created by two bulging and one unpaired adenines. In both sites, hydroxyl and ammonium side chains of the **antibiotic** form 13 direct hydrogen bonds to bases and backbone atoms of the A site. In the best-defined site, 8 water molecules mediate 12 other hydrogen bonds between the RNA and the antibiotics. Ring I of paromomycin stacks over base G1491 and forms pseudo-Watson-Crick contacts with A1408. Both the hydroxyl group and one ammonium group of ring II form direct and water-mediated hydrogen bonds to the U1495oU1406 pair. The bulging conformation of the two adenines A1492 and A1493 is stabilized by hydrogen bonds between phosphate oxygens and atoms of rings I and II. The hydrophilic sites of the bulging A1492 and A1493 contact the shallow groove of G=C pairs in a symmetrical complex. CONCLUSIONS: Water molecules participate in the binding specificity by exploiting the **antibiotic** hydration shell and the typical RNA water hydration patterns. The observed contacts rationalize the protection, mutation, and resistance data. The crystal packing mimics the intermolecular contacts induced by aminoglycoside binding in the ribosome.

L18 ANSWER 2 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1998328824 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9662506
TITLE: Specificity of aminoglycoside antibiotics for the A-site of the decoding region of ribosomal RNA.
AUTHOR: Wong C H; Hendrix M; Priestley E S; Greenberg W A
CORPORATE SOURCE: Department of Chemistry and the Skaggs Institute of Chemical Biology The Scripps Research Institute 10550 North Torrey Pines Road, La Jolla, CA 92037, USA. wong@scripps.edu
SOURCE: Chemistry & biology, (1998 Jul) 5 (7) 397-406.
Journal code: 9500160. ISSN: 1074-5521.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980828
Last Updated on STN: 19980828
Entered Medline: 19980818

AB BACKGROUND: Aminoglycoside antibiotics bind to the A-site of the decoding region of 16S RNA in the bacterial ribosome, an interaction that is probably responsible for their activity. A detailed study of the specificity of aminoglycoside binding to A-site RNA would improve our understanding of their mechanism of **antibiotic** activity. RESULTS: We have studied the **binding** specificity of several aminoglycosides with model RNA sequences derived from the **16S ribosomal** A-site using surface plasmon resonance. The 4,5-linked (neomycin) class of aminoglycosides showed specificity for wild-type A-site sequences, but the 4,6-linked class (kanamycins and gentamicins), generally showed poor specificity for the same sequences. Methylation of a cytidine in the target RNA, as found in the Escherichia coli ribosome, had negligible effects on aminoglycoside binding. CONCLUSIONS: Although both 4,5- and 4, 6-linked aminoglycosides target the same ribosomal site, they appear to bind and effect **antibiotic** activity in different manners. The aminoglycosides might recognize different RNA conformations or the interaction might involve different RNA tertiary structures that are not equally sampled in our ribosome-free model. These results imply that models of ribosomal RNA must be carefully designed if the data are expected to accurately reflect biological activity.

L18 ANSWER 3 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1998263168 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9601031
TITLE: rRNA chemical groups required for aminoglycoside binding.
AUTHOR: Blanchard S C; Fourmy D; Eason R G; Puglisi J D
CORPORATE SOURCE: Department of Structural Biology, Stanford University School of Medicine Fairchild Center, California 94305-5400, USA.
CONTRACT NUMBER: R01-GM51266-01A1 (NIGMS)
SOURCE: Biochemistry, (1998 May 26) 37 (21) 7716-24.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980625
Last Updated on STN: 19980625
Entered Medline: 19980612

AB Through an affinity chromatography based modification-interference assay, we have identified chemical groups within Escherichia coli **16S ribosomal** RNA sequence that are required for **binding** the aminoglycoside **antibiotic** paromomycin. Paromomycin was covalently linked to solid support via a nine atom spacer from the 6"'-amine of ring IV, and chemical modifications to an A-site oligonucleotide that disrupted binding were identified. Positions in the RNA oligonucleotide that correspond to G1405(N7), G1491(N7), G1494(N7), A1408(N7), A1493(N7), A1408(N1), A1492(N1), and A1493(N1), as well as the pro-R phosphate oxygens of A1492 and A1493 in 16S rRNA are chemical groups that are essential for a high-affinity RNA-paromomycin interaction. These data are consistent with genetic, biochemical, and structural studies related to neomycin-class antibiotics and provide additional information for establishing an exact model for their interaction with the ribosome.

L18 ANSWER 4 OF 18 MEDLINE on STN
ACCESSION NUMBER: 96183286 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8605174
TITLE: In vitro selection analysis of neomycin binding RNAs with a mutagenized pool of variants of the 16S rRNA decoding region.
AUTHOR: Famulok M; Huttenhofer A
CORPORATE SOURCE: Institut fur Biochemie der Ludwig-Maximilians-Universitat Munchen, Germany.
SOURCE: Biochemistry, (1996 Apr 9) 35 (14) 4265-70.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 19960531
Last Updated on STN: 19960531
Entered Medline: 19960517

AB An in vitro selection for neomycin B **binding** was carried out with an RNA pool containing a 47-nucleotide domain of the decoding region of **16S ribosomal** RNA, mutated at 30% per base position. The degenerate region was comprised of an oligonucleotide analogue ("motif A") of the decoding region in 30S subunits which has previously been shown to interact with the aminoglycoside **antibiotic** neomycin B and tRNA ligands. After five cycles of selection/amplification, RNA sequences were isolated which specifically bound to neomycin B. Cloning and sequencing showed that none of the isolated clones shared primary sequence or secondary structure homology with the decoding region of 16S RNA. Instead, a new set of sequences was isolated which could be folded into a defined hairpin structure designated as motif B. We investigated the affinity of motif A, motif B, the unselected pool RNA, and the corresponding unmutagenized "parent" RNA to neomycin B at different Mg2+ concentrations. Under buffer conditions of low ionic strength all RNAs tested bound nonspecifically to neomycin B. However, motif B bound to neomycin B at Mg2+ concentrations at which binding of the other RNAs tested was significantly lower or not detectable. This is consistent with motif B exhibiting a higher affinity for neomycin B than motif A under these conditions. Motif B has previously been isolated from an in vitro selection to identify RNA sequences with affinity to neomycin B using a completely randomized RNA pool which shared no relationship to motif A. Our results indicate that motif B might represent a highly optimized RNA sequence for neomycin B binding; conversely, the A-site motif in 16S rRNA (motif A) might not be an optimal target for neomycin B recognition.

L18 ANSWER 5 OF 18 MEDLINE on STN
ACCESSION NUMBER: 94250692 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8193163
TITLE: Antisuppression by a mutation in rpsM(S13) giving a shortened ribosomal protein S13.
AUTHOR: Faxen M; Walles-Granberg A; Isaksson L A
CORPORATE SOURCE: Department of Microbiology, Stockholm University, Sweden.
SOURCE: Biochimica et biophysica acta, (1994 May 17) 1218 (1) 27-34.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940707
Last Updated on STN: 19940707
Entered Medline: 19940629

AB The phenotype associated with an rpsM(S13) mutation, originally isolated in Escherichia coli in a selection for pseudoreversion of streptomycin dependence, was studied in strains lacking the original mutations for **antibiotic** dependence. The rpsM mutation gives a decreased translational step time and a reduced growth rate. It functions as a strong antisuppressor to both the serU(Su1) amber suppressor and the trpT(Su9) opal suppressor, whereas the tyrT(Su3) amber suppressor is much less affected. The small ribosomal subunit from the rpsM mutant shows a reduced sedimentation coefficient but is able to form apparently normal 70S ribosomes as judged by ultracentrifugational analysis. Cloning and sequencing show that the rpsM mutation is a CAG to TAG alteration at codon position 100, giving an S13 protein which is shortened by 19 amino acids at its C-terminal end. This implies that the C-terminal domain of the protein that is involved in **binding** to **16S ribosomal** RNA should be affected.

L18 ANSWER 6 OF 18 MEDLINE on STN

ACCESSION NUMBER: 91293096 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1712293
TITLE: A functional pseudoknot in 16S ribosomal RNA.
AUTHOR: Powers T; Noller H F
CORPORATE SOURCE: Sinsheimer Laboratories, University of California, Santa Cruz 95064.
CONTRACT NUMBER: GM-17129 (NIGMS)
SOURCE: EMBO journal, (1991 Aug) 10 (8) 2203-14.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910901
Last Updated on STN: 19960129
Entered Medline: 19910814

AB Several lines of evidence indicate that the universally conserved 530 loop of **16S ribosomal** RNA plays a crucial role in translation, related to the **binding** of tRNA to the ribosomal A site. Based upon limited phylogenetic sequence variation, Woese and Gutell (1989) have proposed that residues 524-526 in the 530 hairpin loop are base paired with residues 505-507 in an adjoining bulge loop, suggesting that this region of 16S rRNA folds into a pseudoknot structure. Here, we demonstrate that Watson-Crick interactions between these nucleotides are essential for ribosomal function. Moreover, we find that certain mild perturbations of the structure, for example, creation of G-U wobble pairs, generate resistance to streptomycin, an **antibiotic** known to interfere with the decoding process. Chemical probing of mutant ribosomes from streptomycin-resistant cells shows that the mutant ribosomes have a reduced affinity for streptomycin, even though streptomycin is thought to interact with a site on the 30S subunit that is distinct from the 530 region. Data from earlier in vitro assembly studies suggest that the pseudoknot structure is stabilized by ribosomal protein S12, mutations in which have long been known to confer streptomycin resistance and dependence.

L18 ANSWER 7 OF 18 EMBASE
on STN
ACCESSION NUMBER: 2002435735 EMBASE
TITLE: Emergence of tetracycline resistance in Helicobacter pylori: Multiple mutational changes in 16S ribosomal DNA and other genetic loci.
AUTHOR: Dailidiene D.; Bertoli M.T.; Miciuleviciene J.; Mukhopadhyay A.K.; Dailide G.; Pascasio M.A.; Kupcinskas L.; Berg D.E.
CORPORATE SOURCE: D.E. Berg, Department of Molecular Microbiology, Campus Box 8230, Washington Univ. Medical School, 4940 Parkview Place, St. Louis, MO 63110, United States. BERG@BORCIM.WUSTL.EDU
SOURCE: Antimicrobial Agents and Chemotherapy, (1 Dec 2002) Vol. 46, No. 12, pp. 3940-3946.
Refs: 50
ISSN: 0066-4804 CODEN: AMACCQ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20021227
Last Updated on STN: 20021227

AB Tetracycline is useful in combination therapies against the gastric pathogen Helicobacter pylori. We found 6 tetracycline-resistant (Tet(r)) strains among 159 clinical isolates (from El Salvador, Lithuania, and India) and obtained the following four results: (i) 5 of 6 Tet(r) isolates contained one or two nucleotide substitutions in one part of the primary tetracycline **binding** site in 16S rRNA (AGA(965-967) [Escherichia coli coordinates] changed to gGA, AGc, guA, or gGc [lowercase letters are used to represent the base changes]), whereas the sixth (isolate Ind75)

retained AGA(965-967); (ii) PCR products containing mutant **16S ribosomal** DNA (rDNA) alleles transformed recipient strains to Tet(r) phenotypes, but transformants containing alleles with single substitutions (gGA and AGc) were less resistant than their Tet(r) parents; (iii) each of 10 Tet(r) mutants of reference strain 26695 (in which mutations were induced with metronidazole, a mutagenic anti-H. pylori agent) contained the normal AGA(965-967) sequence; and (iv) transformant derivatives of Ind75 and of one of the Tet(r) 26695 mutants that had acquired mutant rDNA alleles were resistant to tetracycline at levels higher than those to which either parent strain was resistant. Thus, tetracycline resistance in H. pylori results from an accumulation of changes that may affect tetracycline-ribosome affinity and/or other functions (perhaps porins or efflux pumps). We suggest that the rarity of tetracycline resistance among clinical isolates reflects this need for multiple mutations and perhaps also the deleterious effects of such mutations on fitness. Formally equivalent mutations with small but additive effects are postulated to contribute importantly to traits such as host specificity and virulence and to H. pylori's great genetic diversity.

L18 ANSWER 8 OF 18 EMBASE
on STN

ACCESSION NUMBER: 2000441999 EMBASE
TITLE: RNA as a target for small molecules.
AUTHOR: Sucheck S.J.; Wong C.-H.
CORPORATE SOURCE: C.-H. Wong, Department of Chemistry, Skaggs Inst. for Chemical Biology, Scripps Research Institute, 10550 North Torrey Pines Road, San Diego, CA 92037, United States. wong@scripps.edu
SOURCE: Current Opinion in Chemical Biology, (2000) Vol. 4, No. 6, pp. 678-686.
Refs: 67
ISSN: 1367-5931 CODEN: COCBF4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010105
Last Updated on STN: 20010105

AB Proteins are folded to form a small binding site for catalysis or ligand recognition and this small binding site is traditionally the target for **drug** discovery. An alternative target for potential **drug** candidates is the translational process, which requires a precise reading of the entire mRNA sequence and, therefore, can be interrupted with small molecules that bind to mRNA sequence-specifically. RNA thus presents itself as a new upstream target for **drug** discovery because of the critical role it plays in the life of pathogens and in the progression of diseases. In this post-genomic era, RNA is becoming increasingly amenable to small-molecule therapy as greater structural and functional information accumulates with regard to important RNA functional domains. The study of aminoglycoside antibiotics and their **binding** to **16S ribosomal** RNA has been a paradigm for our understanding of the ways in which small molecules can be developed to affect the function of RNA.

L18 ANSWER 9 OF 18 EMBASE
on STN

ACCESSION NUMBER: 2000178318 EMBASE
TITLE: Measuring dissociation constants of RNA and aminoglycoside antibiotics by electrospray ionization mass spectrometry.
AUTHOR: Sannes-Lowery K.A.; Griffey R.H.; Hofstadler S.A.
CORPORATE SOURCE: S.A. Hofstadler, Ibis Therapeutics, Div. of Isis Pharmaceuticals, Inc., 2292 Faraday Avenue, Carlsbad, CA 92008, United States. shofstadler@sisph.com
SOURCE: Analytical Biochemistry, (1 May 2000) Vol. 280, No. 2, pp. 264-271.

Refs: 30
ISSN: 0003-2697 CODEN: ANBCA2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000615
Last Updated on STN: 20000615

AB Electrospray ionization mass spectrometry (ESI-MS) has been used to determine the dissociation constants (K(D)s) and **binding** stoichiometry for tobramycin and paromomycin with a 27-nucleotide RNA construct representing the A-site of the **16S ribosomal** RNA. K(D) values determined by holding the ligand concentration fixed are compared with K(D) values derived by holding the RNA target concentration fixed. Additionally, the effect of solution conditions such as the amount of organic solvent present and the amount of salt present in the solution on the K(D) measurement is investigated. It is shown that the preferred method for determining dissociation constants using ESI-MS is holding the RNA target concentration fixed below the expected K(D) and titrating the ligand. K(D) measurements should also be carried out at as high as possible salt concentration to minimize nonspecific binding due primarily to electrostatic interactions. For tobramycin, two nonequivalent binding sites were found with K(D1) = 352 nM and K(D2) = 9 μM. For paromomycin, there is only one binding site with K(D) = 52 nM. (C) 2000 Academic Press.

L18 ANSWER 10 OF 18 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000056501 EMBASE
TITLE: Conformational switch in the decoding region of 16S rRNA during aminoacyl-tRNA selection on the ribosome.
AUTHOR: Pape T.; Wintermeyer W.; Rodnina M.V.
CORPORATE SOURCE: M.V. Rodnina, Institute of Molecular Biology, University of Witten/Herdecke, 58448 Witten, Germany. rodnina@uni-wh.de
SOURCE: Nature Structural Biology, (2000) Vol. 7, No. 2, pp. 104-107.
Refs: 22
ISSN: 1072-8368 CODEN: NSBIEW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000224
Last Updated on STN: 20000224

AB **Binding** of aminoglycoside antibiotics to **16S ribosomal** RNA induces a particular structure of the decoding center and increases the misincorporation of near-cognate amino acids. By kinetic analysis we show that this is due to stabilization of the near-cognate codon recognition complex and the acceleration of two rearrangements that limit the rate of amino acid incorporation. The same rearrangement steps are accelerated in the cognate coding situation. We suggest that cognate codon recognition, or near- cognate codon recognition augmented by aminoglycoside binding, promote the transition of 16S rRNA from a 'binding' to a 'productive' conformation that determines the fidelity of decoding.

L18 ANSWER 11 OF 18 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999264672 EMBASE
TITLE: Design and synthesis of new aminoglycoside antibiotics containing neamine as an optimal core structure: Correlation of **antibiotic** activity with in vitro inhibition of translation.
AUTHOR: Greenberg W.A.; Priestley E.S.; Sears P.S.; Alper P.B.;

Rosenbohm C.; Hendrix M.; Hung S.-C.; Wong C.-H.
CORPORATE SOURCE: C.-H. Wong, Department of Chemistry, Skaggs Institute of Chemical Biology, Scripps Research Institute, 10550 North Torrey Pines Road, San Diego, CA 92037, United States
SOURCE: Journal of the American Chemical Society, (21 Jul 1999) Vol. 121, No. 28, pp. 6527-6541.
ISSN: 0002-7863 CODEN: JACSAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990812
Last Updated on STN: 19990812

AB The structure and activity of the pseudodisaccharide core found in aminoglycoside antibiotics was probed with a series of synthetic analogues in which the position of amino groups was varied around the glucopyranose ring. The naturally occurring structure neamine was the best in the series according to assays for in vitro RNA binding and **antibiotic** activity. With this result in hand, neamine was used as a common core structure for the synthesis of new antibiotics, which were evaluated for **binding** to models of the Escherichia coli **16S** A-site **ribosomal** RNA, in vitro protein synthesis inhibition, and **antibiotic** activity. Analysis of RNA binding revealed some correlation between the relative affinity and specificity of RNA binding and antibacterial efficacy. However, the correlation was not linear. This result led us to develop the in vitro translation assay in an effort to better understand aminoglycoside-RNA interactions. A linear correlation between in vitro translation inhibition and **antibiotic** activity was observed. In addition, IC50s in the protein synthesis assay were typically lower than the K(d)s obtained for RNA binding, suggesting that binding of these compounds to intact ribosomes is tighter in these cases than binding to the model RNA oligonucleotides. This reflects possible differences in RNA conformation between intact ribosomes and the free RNA of the model system, or possible high-affinity ribosomal binding sites in addition to the A-site RNA.

L18 ANSWER 12 OF 18 EMBASE
on STN
ACCESSION NUMBER: 1999137626 EMBASE
TITLE: Docking of cationic antibiotics to negatively charged pockets in RNA folds.
AUTHOR: Hermann T.; Westhof E.
CORPORATE SOURCE: E. Westhof, Inst. Biol. Molec./Cellulaire CNRS, UPR 9002, 15 rue Rene Descartes, F-67084 Strasbourg, France. Westhof@ibmc.u-strasbg.fr
SOURCE: Journal of Medicinal Chemistry, (8 Apr 1999) Vol. 42, No. 7, pp. 1250-1261.
Refs: 82
ISSN: 0022-2623 CODEN: JMCMAR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990527
Last Updated on STN: 19990527

AB The binding of aminoglycosides to RNA provides a paradigm system for the analysis of RNA-**drug** interactions. The electrostatic field around three- dimensional RNA folds creates localized and defined negatively charged regions which are potential docking sites for the cationic ammonium groups of aminoglycosides. To explore in RNA folds the electronegative pockets suitable for aminoglycoside binding, we used calculations of the electrostatic field and Brownian dynamics simulations of cation diffusion. We applied the technique on those RNA molecules experimentally known to bind aminoglycosides, namely, two tobramycin

aptamers (Wang, Y.; Rando, R. R. Chemical Biol. 1995, 2, 281-290): the aminoglycoside-**binding** region in **16S ribosomal** RNA (Moazed, S.; Noller, H. F. Nature 1987, 327, 389-394) and the TAR RNA from human immunodeficiency virus (Mei, H.-Y.; et al. Bioorg. Med. Chemical Lett. 1995, 5, 2755-2760). For the aptamers and ribosomal RNA, for which the binding sites of the aminoglycosides are known, a good agreement between negatively charged pockets and the binding positions of the drugs was found. On the basis of variations between neomycin-like and kanamycin-like aminoglycosides in the interaction with the electrostatic field of ribosomal RNA, we propose a model for the different binding specificities of these two classes of drugs. The spatial congruence between the electronegative pockets in RNA folds and binding positions of aminoglycosides was used to dock aminoglycosides to ribosomal and TAR RNAs. Molecular dynamics simulations were used to analyze possible RNA-**drug** interactions. Aminoglycosides inhibit the binding of the viral Tat protein to TAR RNA; however, the **drug**-binding sites are still unknown. Thus, our docking approach provides first structural models for TAR-aminoglycoside complexes. The RNA-**drug** interactions observed in the modeled complexes support the view that the antibiotics might lock TAR in a conformation with low affinity for the Tat protein, explaining the experimentally found aminoglycoside inhibition of the Tat-TAR interaction.

L18 ANSWER 13 OF 18 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1998309515 EMBASE
TITLE: A library approach to the discovery of small molecules that recognize RNA: Use of a 1,3-hydroxyamine motif as core.
AUTHOR: Wong C.-H.; Hendrix M.; Manning D.D.; Rosenbohm C.; Greenberg W.A.
CORPORATE SOURCE: C.-H. Wong, Department of Chemistry, Skaggs Inst. for Chemical Biology, Scripps Research Institute, 10550 North Torrey Pines Road, San Diego, CA 92037, United States
SOURCE: Journal of the American Chemical Society, (26 Aug 1998) Vol. 120, No. 33, pp. 8319-8327.
ISSN: 0002-7863 CODEN: JACSAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19981022
Last Updated on STN: 19981022

AB A library of compounds based upon an aminoglucopyranoside core has been developed and screened for **binding** to RNA and specifically to **16S ribosomal** RNA. The title molecules simplify the complexity of naturally occurring aminoglycoside antibiotics by embodying a putative recognition motif found within these structures, namely, a 1,3-hydroxyamine. The core pyranoside bearing the hydroxyamine motif was structurally varied at two points through a combinatorial approach utilizing acylation and reductive amination protocols. The aminoglycoside mimetics were screened in an automated assay based upon surface plasmon resonance (SPR), and some were found effective at binding a 27-nucleotide model (AS-wt) of A-site 16S RNA as well as a **drug**- resistant mutant RNA in the micromolar range.

L18 ANSWER 14 OF 18 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 91250767 EMBASE
DOCUMENT NUMBER: 1991250767
TITLE: Mutations in the 915 region of Escherichia coli **16S ribosomal** RNA reduce the **binding** of streptomycin to the ribosome.
AUTHOR: Leclerc D.; Melancon P.; Brakier-Gingras L.
CORPORATE SOURCE: Departement de Biochimie, Universite de Montreal,Montreal H3C 3J7, Canada
SOURCE: Nucleic Acids Research, (1991) Vol. 19, No. 14, pp. 3973-3977.

ISSN: 0305-1048 CODEN: NARHAD
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
022 Human Genetics
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 911216
Last Updated on STN: 911216

AB The nine possible single-base substitutions were produced at positions 913 to 915 of the 16S ribosomal RNA of Escherichia coli, a region known to be protected by streptomycin [Moazed,D. and Noller,H.F. (1987) Nature, 327, 389-394]. When the mutations were introduced into the expression vector pKK3535, only two of them (913A→G and 915A→G) permitted recovery of viable transformants. Ribosomes were isolated from the transformed bacteria and were assayed for their response to streptomycin in poly(U)- and MS2 RNA-directed assays. They were resistant to the stimulation of misreading and to the inhibition of protein synthesis by streptomycin, and this correlated with a decreased binding of the **drug**. These results therefore demonstrate that, in line with the footprinting studies of Moazed and Noller, mutations in the 915 region alter the interaction between the ribosome and streptomycin.

L18 ANSWER 15 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:253521 BIOSIS
DOCUMENT NUMBER: PREV199800253521
TITLE: Binding of neomycin-class aminoglycoside antibiotics to the A-site of 16 S rRNA.
AUTHOR(S): Fourmy, Dominique; Recht, Michael I.; Puglisi, Joseph D. [Reprint author]
CORPORATE SOURCE: Center Molecular Biol. RNA, Univ. California, Santa Cruz, CA 95064, USA
SOURCE: Journal of Molecular Biology, (March 27, 1998) Vol. 277, No. 2, pp. 347-362. print.
CODEN: JMOBAK. ISSN: 0022-2836.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jun 1998
Last Updated on STN: 9 Jun 1998

AB Aminoglycoside antibiotics that bind to ribosomal RNA in the aminoacyl-tRNA site (A-site) cause misreading of the genetic code and inhibit translocation. We have recently solved the structure of an A-site RNA-paromomycin complex. The structure suggested that rings I and II, common to all aminoglycosides that bind to the A-site, are the minimum motif for specific ribosome binding to affect translation. This hypothesis was tested biochemically and with a detailed comparative NMR study of interaction of the aminoglycosides paromomycin, neomycin, ribostamycin, and neamine with the A-site RNA. Our NMR data show that rings I and II of neomycin-class aminoglycosides are sufficient to confer specificity to the binding of the antibiotics to the model A-site RNA. Neomycin, paromomycin, ribostamycin and neamine bind in the major groove of the A-site RNA in a unique binding pocket formed by non-canonical base pairs and a bulged nucleotide. Similar NMR properties of the RNA and the diverse antibiotics within the different complexes formed with neomycin, paromomycin, ribostamycin and neamine suggest similar structures for these complexes.

L18 ANSWER 16 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1998:253520 BIOSIS
DOCUMENT NUMBER: PREV199800253520
TITLE: Paromomycin binding induces a local conformational changes in the A-site of 16 S rRNA.
AUTHOR(S): Fourmy, Dominique; Yoshizawa, Satoko; Puglisi, Joseph D. [Reprint author]
CORPORATE SOURCE: Center Molecular Biol. RNA, Univ. California, Santa Cruz,

CA 95064, USA
SOURCE: Journal of Molecular Biology, (March 27, 1998) Vol. 277, No. 2, pp. 333-345. print.
CODEN: JMOBAK. ISSN: 0022-2836.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jun 1998
Last Updated on STN: 12 Aug 1998

AB Aminoglycoside antibiotics that bind to ribosomal RNA in the amino-acyl-tRNA site (A-site) cause misreading of the genetic code and inhibit translocation. An A-site RNA oligonucleotide specifically binds to aminoglycoside antibiotics and the structure of the RNA-paromomycin complex was previously determined by nuclear magnetic resonance (NMR) spectroscopy. Here, the A-site RNA structure in its free form has been determined using heteronuclear NMR and compared to the structure of the paromomycin-RNA complex. As in the complex with paromomycin, the asymmetric internal loop is closed by a Watson-Crick base-pair (C1407cntdotG1494) and by two non-canonical base-pairs (U1406cntdotU1495, A1408cntdotA1493). A1492 stacks below A1493 and is intercalated between the upper and lower stems. The comparison of the free and bound conformations of the RNA shows that two universally conserved residues of the A site of 16 S rRNA, A1492 and A1493, are displaced towards the minor groove of the RNA helix in presence of **antibiotic**. These changes in the RNA conformation place the N1 positions of A1492 and A1493 on the minor groove side of the A-site RNA and suggest a mechanism of action of aminoglycosides on translation.

L18 ANSWER 17 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:331504 BIOSIS
DOCUMENT NUMBER: PREV199497344504
TITLE: Use of a diffusion gradient chamber to isolate aromatic-degrading microorganisms from the oil-brine contaminated soil.
AUTHOR(S): Emerson, D.; Chauhan, S.; Oriel, P.; Breznak, J. A.
CORPORATE SOURCE: Mich. State Univ., East Lansing, MI, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1994) Vol. 94, No. 0, pp. 256.
Meeting Info.: 94th General Meeting of the American Society for Microbiology. Las Vegas, Nevada, USA. May 23-27, 1994.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Aug 1994
Last Updated on STN: 2 Aug 1994

L18 ANSWER 18 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1991:44682 BIOSIS
DOCUMENT NUMBER: PREV199140021662; BR40:21662
TITLE: EFFECTS OF MUTAGENESIS OF C912 IN THE STREPTOMYCIN **BINDING** REGION OF ESCHERICHIA-COLI **16S RIBOSOMAL** RNA.
AUTHOR(S): FRATTALI A L [Reprint author]; FLYNN M K; DE STASIO E A; DAHLBERG A E
CORPORATE SOURCE: SECT OF BIOCHEM, BROWN UNIV, PROVIDENCE, RI 02912, USA
SOURCE: Biochimica et Biophysica Acta, (1990) Vol. 1050, No. 1-3, pp. 27-33.
Meeting Info.: EMBO (EUROPEAN MOLECULAR BIOLOGY ASSOCIATION), FEBS (FEDERATION OF EUROPEAN BIOCHEMICAL SOCIETIES), AND IUB (INTERNATIONAL UNION OF BIOCHEMISTRY) ADVANCED COURSE ON MECHANISM AND CONTROL OF TRANSLATION, NOORDWIJKERHOUT, NETHERLANDS, MAY 12-17, 1990. BIOCHIM BIOPHYS ACTA.
CODEN: BBACAQ. ISSN: 0006-3002.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR

LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 5 Jan 1991
Last Updated on STN: 9 Jan 1991

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